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<p>(21) International Application Number: <b>PCT/US94/10175</b></p> <p>(22) International Filing Date: <b>7 September 1994 (07.09.94)</b></p> <p>(36) Priority Data: <b>08/116,908 7 September 1993 (07.09.93) US</b></p> <p>(71) Applicant: <b>ESCALON OPHTHALMICS, INC. [US/US]; 182 Teterack Circle, Skillman, NJ 08558 (US).</b></p> <p>(72) Inventor: <b>BENEDETTO, Dominick, A.; 124 Avenue B, Bayonne, NJ 07002 (US).</b></p> <p>(74) Agent: <b>SAUNDERS, Thomas, M.; Lorusso &amp; Lead, 440 Commercial Street, Boston, MA 02109 (US).</b></p>		<p>(81) Designated States: <b>CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).</b></p> <p><b>Published</b> <i>With international search report.</i></p>	

(54) Title: **SURFACE ACTIVE VISCOELASTIC SOLUTIONS FOR OCULAR USE**

## (57) Abstract

This invention encompasses a modified tricopolysaccharide solution for use as a biologically active therapeutic infusion comprising a pharmaceutical grade viscoelastic fraction selected from a group consisting of an acyl-substituted hyaluronic acid having acyl groups thereof with three to twenty carbon atoms and mixtures of said acyl-substituted hyaluronic acid with hyaluronic acid, and hydroxypropylmethylcellulose. In particular these solutions have a surface tension of between 40 and 65 dynes/cm<sup>2</sup>; particularly a viscoelastic fraction has an average molecular weight of at least 50,000. In some embodiments a physiological buffer fraction is present. This invention further encompasses a method of using the claimed composition.

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1        SURFACE ACTIVE VISCOELASTIC SOLUTIONS FOR OCULAR USE

2

3        This application is a continuation-in-part of copending  
4        U.S. Pat. App. 08/061,773 filed May 13, 1993, which is a  
5        continuation of U.S. Pat. App. 07/440,078 filed November 22,  
6        1989, now abandoned.

7

8        **Field of the Invention.**

9        The present invention relates to ophthalmic solutions for  
10      use during ocular and intraocular surgery, and more particularly  
11      to the use of surface active viscoelastic solutions during the  
12      extraction of a cataractous human lens and the implantation of a  
13      prosthetic ocular and intraocular lens. During surgery, the use  
14      of ophthalmic infusions with controlled physical properties,  
15      especially surface activity and viscoelastic properties, is  
16      advantageous for (1) replacing the fluid aqueous humor or ocular  
17      and intraocular air, (2) protecting the internal structures of  
18      the eye from accidental instrument or ocular and intraocular  
19      prosthetic device contact, (3) preventing irrigation damage by  
20      solutions used in routine cataract surgery, and (4) retarding  
21      aspiration from the eye of the viscoelastic solution during the  
22      surgical procedure. In addition, the invention relates to a  
23      method of adhering a contact lens to the surface of the eye,  
24      such as in association with procedures permitting a medical  
25      professional to view ocular and intraocular structures through  
26      the contact lens and through the viscoelastic solution. In  
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1 another application, the viscoelastic solution of this invention  
2 is used by injecting the solution into or under tissues within  
3 the eye, such as to dissect tissue off of the retina.

4                              Background of the Invention

5                              In the past, biocompatible polymers used in ocular and  
6 intraocular surgery have been the naturally occurring  
7 mucopolysaccharides hyaluronic acid and chondroitin sulfate;  
8 mixtures of hyaluronic acid and chondroitin sulfate; and,  
9 cellulose derivatives, such as hydroxypropylmethylcellulose  
10 (HPMC). Table 1

11 presents data reported in Viscoelastic Materials, Ed. E.S.  
12 Rosen, Proceedings of the Second International Symposium of the  
13 Northern Eye Institute, Manchester [U.K.], 17-19 July, 1986  
14 (Pergamon Press, New York) as to the molecular weight of  
15 commercially available ocular products. Depending on the source  
16 from which these mucopolysaccharides are drawn, the molecular  
17 weights are estimated in the 50,000 range with the hyaluronic  
18 acid extending upwards to the  $8 \times 10^6$  range. Hyaluronic acid  
19 was first isolated and characterized by Meyer, Palmer and  
20 reported in the J. Biol. Chem., Vol. 107, p. 629 (1934) and Vol.  
21 114, p. 689 (1936) and by Balazs in the Fed. Proc. Vol. 17, p.  
22 1086 (1958); and chondroitin sulfate by Bray et al. in Biochem.  
23 J. Vol. 38, p. 144 (1944); and Patat, Elias, Z. Physiol. Chem.  
24 vol. 316, p. 1 (1959).

25  
26                              Literature in the art describes the basic isolation and  
27 characterization of the viscoelastic solutions. It is a  
28 surprising feature of this invention which describes the control

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1 of viscoelastic properties as related to the surface activity,  
2 or the solution fracturing under applied stress. In particular,  
3 it is surprising to manipulate or enhance the physical  
4 properties of viscoelastic solutions of mucopolysaccharides,  
5 hyaluronic acid, and/or chondroitin sulfate. It is believed  
6 that disclosure here of a processes to provide hyaluronic acid  
7 and species thereof with controlled surface activity is unique.  
8 This is also especially true of the control of surface activity  
9 of mucopolysaccharide solutions by the addition of biologically  
10 compatible surfactants. A characteristic feature of  
11 biologically compatible surfactants is the absence of observed  
12 alteration in cellular physiology upon contact. Early work in  
13 the viscoelastic field was presented by the inventor of this  
14 disclosure and his associates. Benedetto, D.A. et. al.,  
15 Viscoelastic Materials: Basic Science and Clinical Application,  
16 (Symposium Proceedings), University of Manchester, England, July  
17 17-19, 1986.

18  
19 As to commercial production, a review of the ophthalmic  
20 pharmacopoeia reveals there are several viscoelastic solutions  
21 produced for ocular and intraocular use during ophthalmic  
22 surgery. The most common application for these solutions is in  
23 the intraocular lens implant procedure for human cataract  
24 surgery. This procedure involves extraction of the cataractous  
25 human lens through a small surgical opening in the eye and the  
26 replacement of the lens by a prosthetic intraocular lens placed  
27 in situ. Biocompatible polymers presently or previously in use  
28 are hyaluronic acid (Healon™, Amvisc™); chondroitin sulfate, and

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1 a combined solution of hyaluronic acid and chondroitin sulfate  
2 (Viscoat™); and a hydroxypropylmethylcellulose solution  
3 (Occucoat™). Research conducted recently demonstrates that  
4 Healon™ and Amvisc™ are not surface active, but Viscoat™ and  
5 Occucoat™ are.

6 Chondroitin sulfate does not exist as a free polysaccharide  
7 in its native state, but as a proteoglycan. It is obtained from  
8 sources associated with protein contaminants. The avoidance of  
9 chondroitin sulfate avoids a potential source of pyrogenic  
10 reaction, and the substantial cost associated with protein  
11 removal.

12    Summary of the Invention  
13

14    The invention presented herein discloses modified  
15 mucopolysaccharide or viscoelastic solutions for use as  
16 biologically active therapeutic infusions. In one form of the  
17 invention, the mucopolysaccharide solution is formed from a  
18 viscoelastic fraction and a buffer fraction. It has been found  
19 that when a new synthetic molecule acyl-substituted hyaluronic  
20 acid is employed as the viscoelastic fraction, control of  
21 surface activity is achieved. An indicia of this is the  
22 decrease of the surface tension of the solution which is now  
23 within predetermined limits discussed below. Surface tension  
24 modification is also accomplished with viscoelastic fractions in  
25 which the acyl-substituted hyaluronic acid is mixed with one or  
26 more of hyaluronic acid; and hydroxypropylmethylcellulose. In  
27 certain applications, the viscoelastic solution of this  
28 invention is used in a method of adhering a contact lens to the

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1 surface of the eye, such as in association with procedures  
2 permitting a medical professional to view ocular and intraocular  
3 structures through the contact lens and through the viscoelastic  
4 solution. This is particularly useful in facilitating surgical  
5 procedures. In another application, the viscoelastic solution of  
6 this invention is used by injection the solution into or under  
7 structures or tissues within the eye, such as to dissect tissue  
8 off of the retina.

9  
10 In the broadest terms, surface active viscoelastic  
11 solutions with controlled solution properties, are characterized  
12 by surface tension, equilibrium contact angle, dynamic  
13 viscosity, and cohesiveness (the measure of solution fracture  
14 under stress). In a particular embodiment, this invention is  
15 delimited by the three dimensional representation of Fig. 7.

16 In one example, bioengineered hyaluronic acid from a  
17 bacterial source with an average molecular weight of 50,000 is  
18 modified by acyl substitution with three to twenty carbon atom  
19 acyl groups so that the resultant surface tension of such a  
20 solution is between 40 and 65 dynes/cm<sup>2</sup>. In the practice of  
21 this invention, a viscoelastic solution having a surface tension  
22 of less than about 56 dynes/cm<sup>2</sup>, and more particularly, less  
23 than about 50 dynes/cm<sup>2</sup> is of particular advantage.

24  
25 This invention comprises a modified mucopolysaccharide  
26 solution for use as a biologically active therapeutic infusion  
27 comprising:

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1        a pharmaceutical grade viscoelastic fraction selected from  
2        the group consisting of acyl-substituted hyaluronic acid having  
3        acyl groups thereof with three to twenty carbon atoms,  
4        hyaluronic acid, hydroxypropylmethylcellulose and mixtures  
5        thereof, and absent chondroitin sulfate said fraction having a  
6        surface tension of between 40 and 65 dynes/cm<sup>2</sup>; and,

7        optionally with a physiological buffer fraction, such that  
8        the viscoelastic comprises about a 0.1% percent of the solution  
9        to about 5% of the solution, by weight, and preferably from  
10      about 0.5 % to about 3%;

11        said modified mucopolysaccharide solution having a  
12      viscosity of between 10,000 and 100,000 centipoise when measured  
13      at a shear rate of 3 sec<sup>-1</sup> at 25°C; and,

14        optionally wherein the modified mucopolysaccharide  
15      solution has a surface tension of less than about 56 dynes/cm<sup>2</sup>,  
16      and further a surface tension of less than about 50 dynes/cm<sup>2</sup>;  
17      and further,

18        optionally wherein the solution has an osmolality of from  
19      about 250 to about 400 milliosmoles, or is generally isotonic  
20      with ophthalmic tissue.

21        In some embodiments the modified mucopolysaccharide  
22      solution viscoelastic fraction has an average molecular weight  
23      of at least 50,000. Reference is further made to the  
24      viscoelastic fraction being an acyl-substitute hyaluronic acid  
25      having acyl groups thereof with three to twenty carbon atoms.

26        In particular applications the modified mucopolysaccharide  
27      solution of this invention includes a surfactant fraction of a  
28      biocompatible component selected from a group consisting of

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1 phospholipids, monoglycerides, free fatty acids, free fatty acid  
2 soaps, cholesterol, fluorocarbons, silicones, and nonionic  
3 surfactants, with the surfactant present in an amount sufficient  
4 to produce the required surface tension. In particular, a  
5 biological surfactant fraction of a free fatty acid is present  
6 in an amount of less than 1 mg/ml. Further embodiments include  
7 a surfactant fraction of a biocompatible component selected from  
8 a group consisting of phospholipids, monoglycerides, free fatty  
9 acids, free fatty acid soaps, cholesterol, fluorocarbons,  
10 silicones, and nonionic surfactants, said surfactant present in  
11 an amount less than 10 micrograms/ml. In a preferred embodiment  
12 the surfactant fraction of biocompatible component is a free  
13 fatty acid.

14 In a further embodiment the modified mucopolysaccharide  
15 solution has a viscoelastic fraction of a mixture of  
16 acyl-substituted hyaluronic acid and hyaluronic acid, and  
17 particularly with a surfactant fraction of a biocompatible  
18 component selected from a group consisting of phospholipids,  
19 monoglycerides, free fatty acids, free fatty acid soaps,  
20 cholesterol, fluorocarbons, silicones, and nonionic surfactants,  
21 with surfactant present in an amount sufficient to produce the  
22 required surface tension, usefully in an amount less than  
23 10 micrograms/ml. Preferred surfactants are free fatty acids  
24 such as oleic acid.

25 Particular modified mucopolysaccharide solutions of the  
26 invention are characterized by aspiration through a 0.3 mm  
27 cannula at a vacuum pressure in a range of 5 to 400 mm Hg, and  
28 particularly in a range of 50 to 200 mm Hg, wherein the solution

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1 is easily fractured. Similarly, those solutions with an  
2 aspiration profile of from about horizontal up to about 1.5 and  
3 more particularly from about horizontal to about 1.0 are  
4 preferred.

5 In another embodiment this present invention comprises a  
6 modified mucopolysaccharide solution for use during ophthalmic  
7 surgery for protection of the internal ocular structures  
8 including corneal endothelium from accidental touch by surgical  
9 instruments, yet permitting of observation of said structures  
10 comprising:

11 an optically clear polymeric fraction of high purity  
12 mucopolysaccharides selected from the group consisting of  
13 acyl-substituted hyaluronic acid having acyl groups thereof with  
14 three to twenty carbon atoms, hyaluronic acid,  
15 hydroxypropylmethylcellulose and mixtures thereof and absent  
16 chondroitin sulfate, said fraction having a surface tension of  
17 between 40 and 65 dynes/cm<sup>2</sup>; and,

18 optionally a physiological buffer fraction, such that the  
19 viscoelastic comprises about a 0.1% percent of the solution to  
20 about 5% of the solution, by weight, and preferably from about  
21 0.5 % to about 3%;

22 said modified mucopolysaccharide solution having a  
23 viscosity of between 10,000 and 100,000 centipoise when measured  
24 at a shear rate of 3 sec<sup>-1</sup> at 25 C; and,

25 wherein said mucopolysaccharide fraction has an average  
26 molecular weight of at least 50,000; and,

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1        a biological surfactant fraction of a free fatty acid  
2    present in an amount less than 10 micrograms/ml; and,  
3        optionally wherein the modified mucopolysaccharide  
4    solution has a surface tension of less than about 56 dynes/cm<sup>2</sup>,  
5    and further a surface tension of less than about 50 dynes/cm<sup>2</sup>.

6        In some embodiment of this modified mucopolysaccharide  
7    solution a particular polymeric fraction is hyaluronic acid.

8        Particular modified mucopolysaccharide solutions of the  
9    invention are characterized by aspiration through a 0.3 mm  
10   cannula at a vacuum pressure in a range of 5 to 400 mm Hg, and  
11   particularly in a range of 50 to 200 mm Hg, wherein the solution  
12   is easily fractured, which optionally include those solutions  
13   with an aspiration profile of from about horizontal up to about  
14   1.5 and more particularly from about horizontal to about 1.0.  
15

16       Another embodiment of the present invention includes a  
17   pharmaceutically acceptable modified mucopolysaccharide solution  
18   (particularly a surface active mucopolysaccharide) absent  
19   chondroitin sulfate having a surface tension of between 40 and  
20   65 dynes/cm<sup>2</sup>; and,

21       a viscosity of between 10,000 and 100,000 centipoise  
22   (particularly an average molecular weight of at least 50,000)  
23   when measured at a shear rate of 3 sec<sup>-1</sup> at 25 C.

24       optionally wherein the modified mucopolysaccharide  
25   solution has a surface tension of less than about 56 dynes/cm<sup>2</sup>,  
26   and further a surface tension of less than about 50 dynes/cm<sup>2</sup>.

27       In this embodiment of a modified mucopolysaccharide  
28   solution a particular polymeric fraction is hyaluronic acid.

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1        In certain applications the mucopolysaccharide solution  
2 further comprises a biological surfactant selected from a group  
3 consisting of phospholipids, monoglycerides, free fatty acids,  
4 free fatty acid soaps, cholesterol, fluorocarbons, silicones,  
5 and nonionic surfactants.

6        Yet a further embodiment of the invention includes a method  
7 of protecting internal ocular structures during ocular surgery  
8 and retarding aspiration of material from the ocular surgery  
9 site by the steps of:

10      intracocularly introducing biologically active therapeutic  
11 infusion amount of a modified mucopolysaccharide solution  
12 comprising:

13      a pharmaceutical grade viscoelastic fraction selected from  
14 the group consisting of acyl-substituted hyaluronic acid having  
15 acyl groups thereof with three to twenty carbon atoms,  
16 hyaluronic acid, hydroxypropylmethylcellulose and mixtures  
17 thereof and absent chondroitin sulfate, said fraction with a  
18 surface tension of between 40 and 65 dynes/cm<sup>2</sup> (particularly  
19 less than about 56 and more particularly less than about 50  
20 dynes/cm<sup>2</sup>); and,

21      optionally a physiological buffer fraction, such that the  
22 viscoelastic comprises about a 0.1% percent of the solution to  
23 about 5% of the solution, by weight, and preferably from about  
24 0.5 % to about 3%;

25      said modified mucopolysaccharide solution having a  
26 viscosity of between 10,000 and 100,000 centipoise when measured  
27 at a shear rate of 3 sec<sup>-1</sup> at 25 C. In such embodiment a  
28

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1 preferred method entails intraocularly introducing biologically  
2 active therapeutic infusion amount of a modified  
3 mucopolysaccharide solution by a syringe of about 1.13 cm<sup>3</sup> in  
4 cross section or less, and optionally about 0.57 cm<sup>3</sup> or less,  
5 and further optionally about 0.16 cm<sup>3</sup>. In certain embodiments a  
6 "sloped" syringe absent sharp reductions in cross sectional area  
7 is useful.

8 Further in this method the invention includes particular  
9 modified mucopolysaccharide solutions characterized by  
10 aspiration through a 0.3 mm cannula at a vacuum pressure in a  
11 range of 5 to 400 mm Hg, and particularly in a range of 50 to  
12 200 mm Hg, wherein the solution is easily fractured. Similarly,  
13 those solutions with an aspiration profile of from about  
14 horizontal up to about 1.5 and more particularly from about  
15 horizontal to about 1.0 are preferred.

16 An additional embodiment of the invention includes a method  
17 of protecting internal ocular structures during ocular surgery  
18 by providing a viscoelastic solution that coats ocular  
19 structures at a surgical site such that aspiration of the  
20 viscoelastic solution is retarded, said method being:

21 intraocularly introducing biologically active therapeutic  
22 infusion amount of a modified mucopolysaccharide solution absent  
23 chondroitin sulfate and having a surface tension of between 40  
24 and 65 dynes/cm<sup>2</sup> (particularly less than about 56 and more  
25 particularly less than about 50 dynes/cm<sup>2</sup>) ; and,

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1        a viscosity of between 10,000 and 100,000 centipoise when  
2 measured at a shear rate of 3 sec<sup>-1</sup> at 25 C. In such embodiment  
3 a preferred method entails intraocularly introducing  
4 biologically active therapeutic infusion amount of a modified  
5 mucopolysaccharide solution by a syringe of about 1.13 cm<sup>2</sup> in  
6 cross section or less, and optionally about 0.57 cm<sup>2</sup> or less,  
7 and further optionally about 0.16 cm<sup>2</sup>.

8        Further in this method the invention includes particular  
9 modified mucopolysaccharide solutions characterized by  
10 aspiration through a 0.3 mm cannula at a vacuum pressure in a  
11 range of 5 to 400 mm Hg, and particularly in a range of 50 to  
12 200 mm Hg, wherein the solution is easily fractured. Similarly,  
13 those solutions with an aspiration profile of from about  
14 horizontal up to about 1.5 and more particularly from about  
15 horizontal to about 1.0 are preferred.

16       A next method of the present invention includes a method of  
17 protection of internal ocular structures including corneal  
18 endothelium from accidental touch by surgical instruments, yet  
19 permitting of observation of said structures comprising:

20       intraocularly introducing a modified mucopolysaccharide  
21 solution during ophthalmic surgery wherein said solution  
22 comprises

23       an optically clear polymeric fraction of high purity  
24 mucopolysaccharides selected from the group consisting of  
25 acyl-substituted hyaluronic acid having acyl groups thereof with  
26 three to twenty carbon atoms, hyaluronic acid,  
27 hydroxypropylmethylcellulose and mixtures thereof and absent  
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1 chondroitin sulfate, said fraction having a surface tension of  
2 between 40 and 65 dynes/cm<sup>2</sup> (particularly less than about 56 and  
3 more particularly less than about 50 dynes/cm<sup>2</sup>); and,  
4       optionally a physiological buffer fraction, such that the  
5 viscoelastic comprises about a 0.1% percent of the solution to  
6 about 5% of the solution, by weight, and preferably from about  
7 0.5 % to about 3%;  
8       said modified mucopolysaccharide solution having a  
9 viscosity of between 10,000 and 100,000 centipoise when measured  
10 at a shear rate of 3 sec<sup>-1</sup> at 25 C; and,  
11      wherein said mucopolysaccharide fraction has an average  
12 molecular weight of at least 50,000; and,  
13      a biological surfactant fraction of a free fatty acid  
14 present in an amount less than 10 micrograms/ml.  
15 In such embodiment a specific method entails intraocularly  
16 introducing biologically active therapeutic infusion amount of a  
17 modified mucopolysaccharide solution by a syringe of about 1.13  
18 cm<sup>2</sup> in cross section or less, and optionally about 0.57 cm<sup>2</sup> or  
19 less, and further optionally about 0.16 cm<sup>2</sup>.  
20 Further in this method the invention includes particular  
21 modified mucopolysaccharide solutions characterized by  
22 aspiration through a 0.3 mm cannula at a vacuum pressure in a  
23 range of 5 to 400 mm Hg, and particularly in a range of 50 to  
24 200 mm Hg, wherein the solution is easily fractured. Similarly,  
25 those solutions with an aspiration profile of from about  
26 horizontal up to about 1.5 and more particularly from about  
27 horizontal to about 1.0 are preferred.  
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1        A next embodiment of the invention comprises a modified  
2 mucopolysaccharide solution for use as a biologically active  
3 therapeutic infusion comprising:

4        a pharmaceutical grade viscoelastic fraction selected from  
5 the group consisting of acyl-substituted hyaluronic acid having  
6 acyl groups thereof with three to twenty carbon atoms,  
7 hyaluronic acid, hydroxypropylmethylcellulose and mixtures  
8 thereof, and absent chondroitin sulfate said fraction having a  
9 surface tension of between 40 and 65 dynes/cm<sup>2</sup> (particularly  
10 less than about 56 and more particularly less than about 50  
11 dynes/cm<sup>2</sup>); and,

12        said modified mucopolysaccharide solution having a  
13 viscosity of between 10,000 and 100,000 centipoise when measured  
14 at a shear rate of 3 sec<sup>-1</sup> at 25°C.

15        This invention encompasses a modified mucopolysaccharide  
16 solution for use as a biologically active therapeutic infusion  
17 comprising:

18        a pharmaceutical grade viscoelastic fraction selected from  
19 a group consisting of an acyl-substituted hyaluronic acid having  
20 acyl groups thereof with three to twenty carbon atoms and  
21 mixtures of said acyl-substituted hyaluronic acid with  
22 hyaluronic acid, chondroitin sulfate A, chondroitin sulfate B,  
23 chondroitin sulfate C, and hydroxypropylmethylcellulose, said  
24 fraction with a surface tension of between 40 and 65 dynes/cm<sup>2</sup>;  
25 particularly a viscoelastic fraction has an average molecular  
26 weight of at least 50,000; and,

27

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1       optionally a physiological buffer fraction, such that the  
2       viscoelastic comprises about a 0.1% percent of the solution to  
3       about 5% of the solution, by weight, and preferably from about  
4       0.5 % to about 3%;

5       whereby, upon infusion of modified mucopolysaccharide  
6       solution at the site, the surface activity of the solution  
7       enhances coating of the site.

8       A specific modified mucopolysaccharide solution is one with  
9       an acyl-substituted hyaluronic acid, and a preferred viscosity  
10      is between 10,000 and 100,000 centipoise when measured at a  
11      shear rate of 3 sec<sup>-1</sup> at 25°C, and optionally further including  
12      a surfactant fraction of a biocompatible component selected from  
13      a group consisting of phospholipids, monoglycerides, free fatty  
14      acids, free fatty acid soaps, cholesterol, fluorocarbons,  
15      silicones, and nonionic surfactants, said surfactant present in  
16      a trace amount sufficient to produce said surface tension. In  
17      one embodiment the surfactant is present in an amount less than  
18      10 micrograms/ml. A preferred surfactant is oleic acid. A  
19      preferred modified mucopolysaccharide solution comprises a  
20      mixture of an acyl-substituted hyaluronic acid and hyaluronic  
21      acid.

22       In a particular application this invention includes a  
23       modified mucopolysaccharide solution for use a biologically  
24       compatible therapeutic infusion comprising:

25       a pharmaceutical grade viscoelastic fraction selected from  
26       a group consisting of hyaluronic acid, chondroitin sulfate A,  
27       chondroitin sulfate B, and chondroitin sulfate C, said fraction  
28       having an average molecular weight of at least 50,000.

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1        a surfactant fraction of a biocompatible component selected  
2        from a group consisting of phospholipids, monoglycerides, free  
3        fatty acids, free fatty acid soaps, cholesterol, fluorocarbons,  
4        silicones, and nonionic surfactants, said surfactant present in  
5        a trace amount sufficient to produce a surface tension of  
6        between 40 and 65 dynes/cm<sup>2</sup>; and,

7        optionally a physiological buffer fraction, such that the  
8        viscoelastic comprises about a 0.1% percent of the solution to  
9        about 5% of the solution, by weight, and preferably from about  
10      0.5 % to about 3%;

11      whereby, upon infusion of modified mucopolysaccharide  
12      solution at the site, the surface activity of the solution  
13      enhances coating of the site and results in retardation of  
14      aspiration at the site. A preferred modified mucopolysaccharide  
15      solution has a viscoelastic fraction of hyaluronic acid, and,  
16      optionally, a viscosity of between 10,000 and 100,000 centipoise  
17      when measured at a shear rate of 3 sec<sup>-1</sup>, and further  
18      optionally, a surfactant, particularly oleic acid, and  
19      particularly with surfactant present in an amount less than 10  
20      micrograms/ml.

21      In one embodiment this invention includes a modified  
22      mucopolysaccharide solution for use during ophthalmic surgery  
23      for protection of the internal ocular structures comprising:

24      an optically clear polymeric fraction of high-purity  
25      mucopolysaccharides and mixtures thereof, said polymeric  
26      fraction selected from the group consisting of hyaluronic acid,  
27      chondroitin sulfate A, chondroitin sulfate B, chondroitin

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